REMARKS

Claims 19-39 currently appear in this application. The Office Action of January 22, 2004, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Allowed Claims

Claims 19-33 are allowed.

Rejections under 35 U.S.C. 112

Claims 34-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification is said not to reasonably provide enablement for any pH- or potential sensitive fluorophore, without other structural information which interacts with any surface whatsoever.

This rejection is respectfully traversed. Claim 34 requires that the pH or surface potential that is altered is that of the polymer. The fluorophore is covalently attached to the polymer.

One skilled in the art would be conversant with fluorophores which are pH or potential sensitive. A very

brief search on the internet turned up the following, copies of which are submitted herewith:

Demaurex et al., *J. Biol. Chem.* 1998 **273(4)**:2044-2051

Polarity (potential) sensitive dye Based Mechanism from analytik. chemie. Uni. Regensburg.

Sauer et al., *Angewandte Chemic, International Edition* **42(16)**:1790-93, only title enclosed.

Invitrogen Detection Technologies, "Other Nonpolar and Amphiphilic Probes"

The claims as amended define the species, the binding of which is to be determined, and the polymer surface as having opposite charges. The combination of this added feature, with the definition of the fluorophore as pH or potential sensitive, make it clear to one skilled in the art how this method for determining a species at a polymer surface can be effected. There is a wide range of fluorophores that are pH- or potential sensitive. The fluorophore is covalently attached to a polymer surface. When the binding of the species at the polymer surface is effective to alter the pH or the surface potential of the polymer, the fluorescent property of the fluorophore changes. That it, the fluorophore is used to detect changes in the pH or potential in the environment in which the probe is located, these changes due to binding or dissociation of a species.

Claims 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that claims 34 and 35 encompass a genus of fluorophores whose fluorescence is dependent upon the binding or dissociation of a species at a surface, yet only three specific species of such fluorophores are suggested by the specification, namely, those linked to steroids, those linked to sphingolipids, or those lined to lipids having at least two chains of 14 atoms.

The Examiner is concerned that different polymers would operate in similar ways with respect to the fluorophore, and alleges that the disclosure is only narrowly drawn to a particular fluorophore. It is respectfully submitted that this is not the case, as the specification at page 2, beginning at line 4, describes the method as determining the binding of a species at a surface having a local environment at a given pH or surface potential, where the binding is effective to alter the pH or the potential. A pH or potential sensitive fluorophore is stably incorporated at the surface, and a change in a fluorescent property of the fluorophore is observed upon binding or dissociation of the species at the surface due to a change in surface potential or pH. **The method detects changes in the environment of the probe, not necessarily dependent on interactions of the probe with a specific molecule.** [emphasis added] In fact, one embodiment of the invention is the use of a polymer to which the fluorophore is stably bound, and the method comprises

observing a change in a fluorescent property of the fluorophore upon binding or dissociation of a species at the surface of the polymer, due to a change in surface potential or pH. The polymers may be in various forms, such as micro- or nanoparticles, or as sheets, as in cellulose-based polymers. The specification at page 2, beginning at line 25, notes that fluorophores which may be employed in the probe include pH-sensitive lissamine, rhodamine, 7-hydroxycoumarin, fluorescein, and pH- or potential-sensitive derivatives thereof.

What is claimed herein is a method for detecting changes in the environment of the probe, these changes being a change in potential or pH. The specific fluorophore used is not critical, as long as it is a fluorophore which is pH- or potential- sensitive. One skilled in the art can readily determine if a fluorophore is pH- or potential sensitive based upon the large number of fluorophores available which are well described in the literature. Selection of the fluorophore can be accomplished without undue experimentation, as can the polymer surface to which the fluorophore is bound.

The specification at page 7, lines 15-21, defines "pH- or potential-sensitive" fluorophores as those which have one or more fluorescent properties which undergo an observable change upon a change in the electrical potential or pH of the environment. Such properties may include fluorescent intensity, ratio of fluorescent intensities at different excitation or emission wavelengths, fluorescent lifetime, steady state or time dependent fluorescence polarization, etc.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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